Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 2-4, 7-29, 44-47, and 51-52 are pending in the application, with claim 2 being the independent claim. Claims 2, 3, 10, 16-18, 24, 26-28, 44, 51 and 52 have been amended. It is believed these changes introduce no new matter, and their entry is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and request that they be withdrawn.

Claim amendments

Claim 2 has been amended to change, for example, "one or more modifications or mutations at positions corresponding to leucine 52 of M-MLV reverse transcriptase" to "an amino a substitution corresponding to a substitution of leucine 52 of M-MLV reverse transcriptase for a different amino acid." Support for the amendment may be found in the specification, for example, at Table 1, on pages 8-9; page 39, paragraph 0107; and page 41, paragraph 0112.

Claim 2 has also been amended to add the phrase "wherein the retroviral reverse transcriptase is encoded by a nucleic acid that hybridizes to the complement of a nucleic acid encoding a wild type retroviral reverse transcriptase." Support for the amendment may be found in the specification, for example, at page 41, paragraph 0115; and page 30, paragraph 0082.

Claim interpretation

The interpretation given during examination must be of a breadth consistent with the interpretation given by an artisan of ordinary skill. *In re Cortright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999); MPEP 2111 at p. 2100-47 (8th ed., Rev. 1, Feb. 2003). Moreover, claim terms need only be as precise as the art. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

Here, reverse transcriptases are routinely characterized by artisans of ordinary skill as being, for example, "retroviral" or "bacterial." Moreover, one of ordinary skill in the art would not interpret the claim term "*retroviral* reverse transcriptase" to encompass enzymes from *bacteria* such as *T. aquaticus*. Thus, the Office Action's interpretation of the pending claims as encompassing Taq DNA polymerase, in relation to the rejection under 35 U.S.C. § 103, is unreasonable.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 16-18 and 24 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. The Office Action states that it is unclear what is the "corresponding wild type enzyme." Applicants respectfully traverse the rejection.

Claim 2 has been amended to recite a retroviral reverse transcriptase comprising a substitution, wherein the reverse transcriptase is encoded by a nucleic acid that hybridizes to the complement of a nucleic acid encoding a wild type retroviral reverse transcriptase. Claims 16-18 depend from claim 2 and have been amended to change "corresponding wild type enzyme" to "said wild type reverse transcriptase." Thus, it is

clear what is the reference enzyme. The rejection is therefore moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, first paragraph - Written description

Claims 2, 3, 7, 10-18, 24, 26-28, 44-47, 51 and 52 were rejected under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter that was not described in such a way as to reasonably convey that the inventors had possession of the claimed invention at the time the application was filed. Applicants respectfully traverse the rejection.

As recently reiterated by the Federal Circuit, the crux of the question concerning whether a claimed invention is adequately described is whether one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention in the specification as filed. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1320 (Fed. Cir. 2003) (citing *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991)); *see also* M.P.E.P. § 2163.02. The Federal Circuit in *Eli Lilly* set forth several tests for whether a claimed genus is adequately described, including the "representative number of species" test and the "common structural features" test. *Regents of the Univ. of Calif. v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). However, the court also stated that "[w]e will not speculate in what *other ways* a broad genus of genetic material may be properly described." *Id.* (emphasis added).

In fact, subsequent to *Eli Lilly*, the Federal Circuit instructed that *functional* descriptions of biological material can satisfy the written description requirement if a structure/function correlation is known in the art. *See Amgen Inc. v. Hoechst Marion*

Roussel Inc., 314 F.3d 1313, 1332 (Fed. Cir. 2003).[1] The Federal Circuit has also reasoned, in reference to the recitation of known biological materials, that a description of a genus by words alone is sufficient if one of ordinary skill could recognize the members of the genus. *Amgen* at 1332. In *Amgen*, the Federal Circuit refused to apply the "representative number of species" test to the claim term "vertebrate host cell." *Id.* Further, it concluded that the claims at issue were adequately described, even though the specification described *only two species* within the genus. *Id.*[2] In addition, the Federal Circuit and the PTO have acknowledged that a specification may adequately describe a genus even though it fails to describe a single species falling within the genus. *Eli Lilly* at 1406; MPEP 2163 (II)(A)(3)(a)(ii) at p. 2100-169, col. 1.

Thus, there is no fixed set of tests for whether a claimed genus is adequately described. Instead, the determination of compliance with the written description requirement is a fact-based one, and in cases subsequent to *Eli Lilly*, the Federal Circuit has limited the holding in *Eli Lilly* to its particular set of facts. *E.g.*, *Moba* at 1320[3];

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1 "*Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." (citation omitted).

2 "[W]hen used, as here, merely to identify types of cells (instead of undescribed, *previously unknown* DNA sequences), the words 'vertebrate' and 'mammalian' readily 'convey[ ] distinguishing information concerning [their] identity' such that one of ordinary skill in the art could 'visualize or recognize the identity of the members of the genus.'" (quoting from *Eli Lilly*) (emphasis added).

3 "Invoking § 112, *Lilly* required a precise definition of a DNA sequence in the patent specification. *In more recent cases, however, this court has distinguished Lilly.*" (emphasis added).

Amgen at 1332[4]; *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002).

In the present case, the specification clearly conveys that the inventors contemplated the claimed genus of substitution mutants. For example, on page 7, paragraph 0018, the specification generically describes one aspect of the invention as "mutant or modified reverse transcriptases" and lists the preferred sites for mutation within *some* reverse transcriptases (M-MLV, AMV, RSV, and HIV) in Table 1 on page 8. In reference to Table 1, the specification states on page 8, "[s]imilar or equivalent sites or corresponding sites in *other* reverse transcriptases can be mutated or modified to produce additional thermostable reverse transcriptases" (emphasis added). The specification states that "the amino acids at the selected positions may be substituted with any other amino acid" at page 41, paragraph 0112.

The specification describes a number of enzymes that could serve as the backbone for making the recited substitutions. For example, the specification describes reverse transcriptases from M-MLV, HIV, and ASLV as the *prototypical* retroviral reverse transcriptases and describes nine members of the ASLV group, including RSV and AMV on pages 3-4. Publications describing cloned and naturally occurring reverse transcriptases, and nucleic acids encoding such enzymes, are cited and incorporated by reference throughout the specification, for example, at pages 3-4, and page 41, paragraph 0114

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4 "Both *Eli Lilly* and *Enzo Biochem* are inapposite to this case because the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend."

The specification, in the section "Sources of Reverse Transcriptases" on page 32, states that enzymes of the invention include any enzyme having reverse transcriptase activity, including retroviral reverse transcriptases. Also, the same section mentions mutants, fragments, variants and derivatives of reverse transcriptases, and describes how to make such mutants. Assays for reverse transcriptase activity are described throughout the specification, such as in Example 2, starting on page 64. The specification, on page 18, paragraph 0040, describes preferred reverse transcriptases as including single and multi-subunit reverse transcriptases, in particular, M-MLV and ASLV reverse transcriptases. Reverse transcriptases from M-MLV, AMV, RSV, RAV, and MAV, and reverse transcriptases from the ASLV group, in general, are also mentioned in page 32.

As described in the specification on page 37, paragraph 0100, sources of reverse transcriptases of the invention include natural viral sources as well as recombinant sources. Numerous known mutant reverse transcriptases are also described that may serve as the backbone for the recited substitutions. For example, the specification describes known enzymes with reduced RNase H activity and assays for measuring this reduction in activity on page 34, paragraph 0092.

Therefore, the specification describes a broad genus of enzymes, as well as specific examples, that could serve as the backbone for making the recited substitutions of the invention. These "backbone" sequences need not have been provided in the specification because they were known. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94 (holding that the description only needs to describe what is new or not conventional); MPEP 2163, p. 2100-165, col. 2 (Rev. 1, Feb. 2003).

Clearly, one of ordinary skill would have reasonably concluded that the inventors had possession of the claimed substitution mutants when the application was filed. Therefore, the claimed genus was adequately described. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection under 35 U.S.C. § 102 - Blain et al.

Claims 2, 16-18, 24, 26, and 28 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated Blain *et al.* (*J. Biol. Chem. 268*:23585-2392 (1993), PTO-892 document U). Applicants respectfully traverse this rejection.

Independent claim 2 has been amended. Claims 16-18, 24, 26, and 28 depend from claim 2. As amended, the claims are directed to a retroviral reverse transcriptase containing a substitution corresponding to a substitution of a different amino acid for Leu52, His204, Met289, or Thr306 of M-MLV reverse transcriptase.

At a minimum, Blain *et al.* do not teach or suggest the particular substitutions recited in the pending claims. Therefore, the pending claims are novel over Blain *et al.* Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection over Blain *et al.*

Rejection under 35 U.S.C. § 102 - Arakawa et al.

Claims 2, 16-18, 24, 26 and 28 were rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Arakawa *et al.* (Japanese patent application 2000-139457, PTO-892 document N). Applicants respectfully traverse this rejection.

The Office Action is in error concerning the disclosure in Arakawa *et al.* This document does not teach modifications at positions Leu52, His204, Met289, or Thr306

of M-MLV reverse transcriptase. As was known in the art, and stated in the specification, "wild type M-MLV reverse transcriptase is derived by proteolysis from a precursor polyprotein and thus the wild type M-MLV reverse transcriptase does not start with a methionine." Specification, Example 1, paragraph [0161] on page 60. The sequence provided in Arakawa *et al.* includes a methionine residue at the amino terminus. The numbering of the positions pointed to in the Office Action are therefore off by one amino acid from those recited in the claims. The positions pointed to in the Office Action actually correspond to positions Pro51, Leu203, Val288, and Gly305 of M-MLV reverse transcriptase.

Thus, at a minimum, Arakawa *et al.* do not teach or suggest modifications at the positions recited in the claims, and the pending claims are novel over Arakawa *et al.* Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection over Arakawa *et al.*

Rejection under 35 U.S.C. § 102 - Lawyer et al.

Claims 2, 12-18, 24, and 26-28 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Lawyer *et al.* (*J. Biol. Chem. 264*:6427-6437 (1989). Applicants respectfully traverse the rejection.

The pending claims are directed to a retroviral reverse transcriptase containing a substitution corresponding to a substitution of a different amino acid for Leu52, His204, Met289, or Thr306 of M-MLV reverse transcriptase.

Lawyer *et al.* describe a *Taq* DNA transcriptase. At a minimum, Lawyer *et al.* do not teach or suggest a *retroviral* reverse transcriptase. As discussed above in the comments concerning claim interpretation, one of ordinary skill in the art would not

interpret the claim term "*retroviral* reverse transcriptase" to encompass *bacterial* enzymes. Therefore, the claims are novel over Lawyer *et al.* Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection over Lawyer *et al.*

Rejections under 35 U.S.C. § 103

Claims 44-47 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Blain *et al.*, or Arakawa *et al.*, or Lawyer *et al.*, in view of p. 39 of the Stratagene Catalog page 39 (1988). Applicants respectfully traverse the rejection.

Claims 44-47 are directed to a kit comprising a retroviral reverse transcriptase of claim 2.

As discussed above in relation to the rejections under 35 U.S.C. § 102, none of Blain *et al.*, Arakawa *et al.*, or Lawyer *et al.* teaches or suggests all the elements of claim 2. Page 39 of the Stratagene catalog does not remedy this deficiency. Therefore, claims 44-47 are nonobvious over the combination of cited documents. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S. § 103.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will

expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: March 26, 2004

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